AdvanTIG-105: phase 1b dose-expansion study of ociperlimab (OCI) + tislelizumab (TIS) with chemotherapy (chemo) in patients (pts) with stage IV gastric/gastroesophageal adenocarcinoma (GC/GEJC)

Authors: Se Hyun Kim MD,[1] Timothy Clay MD,[2] Sophia Frentzas MD,[3] Gyeong-Won Lee MD,[4] Her-Shyong Shiah MD,[5] Byoung Yong Shim MD,[6] David R Spigel MD,[7] Meili Sun MD,[8] Feng Wang MD,[9] Harry Yoon MD,[10] Wei Tan PhD,[11] Ruihua Wang MD,[11] Hao Zheng PhD,[12] Ziqi Zhou PhD,[11] Yi Ba MD*[13]

*Corresponding author

Affiliations:

1. *Seoul National University Bundang Hospital, Seongnam, Republic of Korea*
2. *St. John of God Subiaco Hospital, Perth, Australia*
3. *Department of Medical Oncology, Monash Heath and Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria, Australia*
4. *Division of Hematology-Oncology, Department of Internal Medicine, Institute of Health Science, Gyeongsang National University Hospital, Gyeongsang National University College of Medicine, Jinju, Korea*
5. *Taipei Tzu Chi Hospital, Taipei City, Taiwan*
6. *The Catholic University of Korea, St. Vincent's Hospital, Suwon, Republic of Korea*
7. *Sarah Cannon Research Institute at Tennessee Oncology PLLC, Nashville, TN, USA*
8. *Jinan Central Hospital, Jinan, China*
9. *The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China*
10. *Mayo Clinic, Rochester, MN, USA*
11. *BeiGene (Shanghai) Co., Ltd., Shanghai, China*
12. *BeiGene (USA) Co., Ltd., San Mateo, CA, USA*
13. *Tianjin Medical University Cancer Institute and Hospital, Tianjin, China*

Background: T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) inhibitor in combination with an anti-programmed cell death protein 1 (PD-1) antibody has shown antitumor activity in solid tumors. AdvanTIG-105 (NCT04047862) is a phase 1/1b open-label study designed to assess the safety and preliminary antitumor activity of OCI, an anti-TIGIT monoclonal antibody (mAb), + TIS, an anti-PD-1 mAb, in pts with unresectable, locally advanced or metastatic solid tumors. In the dose-escalation part, OCI + TIS was well tolerated with preliminary antitumor activity observed, and the recommended phase 2 dose (RP2D) of OCI 900 mg intravenously (IV) every three weeks (Q3W) + TIS 200 mg IV Q3W was established. We report results from the dose-expansion part (GC/GEJC Cohort 9) of the AdvanTIG-105 study.

Methods: Eligible pts had histologically/cytologically confirmed stage IV GC/GEJC. Pts were excluded if they had squamous cell, undifferentiated or other histological types of GC, had GC/GEJC with positive HER2 expression, or if they had received any prior therapy for metastatic disease. Pts received either the RP2D of OCI + TIS with oxaliplatin

+ capecitabine Q3W for 6 cycles (C), followed by maintenance therapy with the RP2D of OCI + TIS, + capecitabine Q3W, or the RP2D of OCI + TIS with cisplatin + 5-fluorouracil Q3W for 6 C. Treatment continued until disease progression, intolerable toxicity, or withdrawal of consent. The primary endpoint was investigator-assessed overall response rate (ORR) per RECIST v1.1. Secondary endpoints included progression-free survival (PFS), duration of response (DoR), disease control rate (DCR) per RECIST v1.1, and safety.

Results: As of September 29, 2022, 60 pts with a median age of 61.5 years (range 35-82) were enrolled; 59 were efficacy evaluable. Median study follow-up was 31.1 weeks (range 1.4-78.4). ORR was 50.8% (95% CI: 37.5, 64.1); DCR was 84.7% (95% CI: 73.0, 92.8) with a median DoR of 4.6 months (95% CI: 3.9, 7.1). Median PFS was 8.2 months (95% CI: 5.8, not evaluable). In a subgroup analysis, ORR in pts with PD-L1 tumor area positivity (TAP) score ≥5% (n=27) was 59.3% (95% CI: 38.8, 77.6), and 50.0% (95% CI: 30.7, 69.4) in pts with PD-L1 TAP <5% (n=28). All 60 pts reported ≥1 treatment-emergent adverse event (TEAE), the most common being anemia (43.3%) and platelet count decreased (41.7%). In total, 43 pts (71.7%) had ≥grade 3 TEAEs and 28 (46.7%) had serious adverse events. TEAEs leading to discontinuation of TIS and OCI occurred in 5 (8.3%) pts. TEAEs led to death in 2 (3.3%) pts; one event (neutropenic sepsis) was related to chemo, while the other (pulmonary embolism) was not treatment related.

Conclusions: OCI 900 mg + TIS 200 mg + chemo was generally well tolerated and showed encouraging antitumor activity in pts with stage IV GC/GEJC.